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An evaluation of the safety of blood product transfusion in children under 18: systematic review

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Abstract

Background: Every year, blood transfusions save countless lives, extend life expectancy, enhance the condition of life of individuals with life-threatening illnesses. The rate of blood transfusion reactions in children is higher than in the general population of adults. As children grow and develop, they are very different from adults regarding how they need to be diagnosed and treated. The present systematic review aimed to evaluate potential adverse consequences and correlations associated with blood transfusions in children.

Methods: A literature search was carried out using PubMed, Scopus, Embase, MEDLINE, CINAHL, Web of Science, and Cochrane. A manual search was also undertaken using reference harvesting in ARU. The literature search was done to cover the duration between 2011 to 2021 using Boolean logic with the following terms: Blood transfusion, Transfusion Safety, Adverse effects/Transfusion, Transfusion reaction, and Children.

Results: The majority of the studies discussed RBC transfusion among critically ill children. They all reach an almost similar opinion that there are adverse effects associated with blood transfusion, especially in immunocompromised children or neonates. Discussions about plasma transfusions also showed the same results. The significant outcomes of the blood transfusion are nosocomial infections, prolonged hospital stay, early mortality, and transfusion-related hyperkalaemia. Although transfusion is a valuable therapy, there is always the possibility of side effects, with a greater occurrence rate in children under the age of 18, thus the healthcare team must respond quickly to minimise problems and control those that do occur.

Conclusions: Acute and chronic diseases usually necessitate blood transfusions. This systematic study emphasises paediatric transfusion responses and shows that the incidence of transfusion reactions among the paediatric population is on the rise. More research is necessary to explain suitable indications and the introduction of standardised protocols for the blood transfusion process and subsequent reactions in children.

Keywords: *blood transfusion, safety, transfusion reaction, children, paediatric transfusion, haemovigilance, paediatrics, adolescents, infants, evidence synthesis*

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Evidence in Context

• Blood transfusions significantly enhance survival and quality of life in complex medical conditions. • Separating blood into components maximizes utility for multiple patients. • Pediatric transfusions require tailored approaches for product type and dosage. • Despite safety advances, adverse reactions in pediatric patients remain concerning. • Continued research and hemovigilance are essential to improve transfusion outcomes.

To view Article

Introduction

Every year, blood transfusions save countless lives, extend life expectancy, enhance the condition of life of individuals with life-threatening illnesses, and aid in completing complicated medical and surgical operations [1]. When unsafe blood is available for transfusion, it has a detrimental influence on the performance of essential health services and programmes responsible for providing proper patient treatment in an extensive variety of acute and chronic illnesses [1]. Globally, more than 112 million blood units are collected annually, and around 14 million units are administered to patients through transfusions each year [2].

It is possible to make efficient use of blood if it is separated into different products such as red cell concentrates, platelet concentrates, plasma, and cryoprecipitates, which will meet the requirements of more than one patient [1]. Transfusion of red blood cells into patients is done to increase their oxygen-carrying capability [3]. In individuals with clinically substantial coagulopathy, plasma transfusion can help restore their health. Patients with thrombocytopenia or platelet dysfunction benefit from transfused platelets because they can prevent or control bleeding. The transfusion of cryoprecipitate is used to treat hypofibrinogenemia [3].

Transfusions are often required in paediatrics, notably in preterm infants, patients with hematologic malignancies or diseases, and severely unwell children in paediatric critical care units [4]. Paediatric patients admitted to high-risk critical care units are about 5% more likely than the general population to get at least one transfusion during their stay [5].

During their growth and development, children differ significantly from adults. They have a unique set of needs that must be considered when making decisions about the type of product, alteration, dosages, rate of administering, and possible side effects of blood transfusions [6-8].

Despite the progress in transfusion safety accomplished through the application of good manufacturing practice (GMP) and ideal treatment protocols, formed elements can cause acute (within 24 hours) or delayed (within 24 hours) adverse effects, particularly in transfusion-dependent paediatric patients [9]. The consequences of a transfusion process may directly impact a child's long-term health, particularly in the case of neurocognitive development in children [10]. The nature and severity of harmful transfusion responses in children who have received blood transfusions differ from those in adults [11]. It is almost transparent that studies showing a reduced utilisation of blood transfusion may be attributed to a positive impact on patient surgical treatment and policies advocating the sensible use of donated blood products in the first place [12,13].

A comprehensive understanding of the many forms of adverse transfusion reactions and their prevalence in this paediatric group is required. However, this remains a considerable problem. Innovative research studies and active hemovigilance are necessary to enhance screening, increase the detection of adverse transfusion events, and encourage the use of new procedures and preventative strategies in clinical practice, all of which will benefit patients [11].

Adverse transfusion responses in children continue to be poorly understood and discussed. How often and in what order unfavourable reactions to blood transfusions occur is still unclear. Uncertainty about the actual nature of the hazards and benefits of blood transfusion can lead to reports of considerable differences in the transfusion technique in children with various blood products. The systematic review aimed to evaluate potential adverse consequences and correlations associated with blood transfusions in children.

Methods

Study Design

This study was designed to provide an inclusive picture of blood transfusion reactions in children. It systematically searched the medical literature and identified all the relevant publications comparing blood transfusion safety in children. The analysis encompassed observational studies of a quantitative nature that presented original empirical findings on the subject matter.

Search Strategy

Following the guidelines published by the "Centre for Reviews and Dissemination (CRD)" in 2009, an initial evaluation of the current studies was undertaken to substantiate this systematic review's necessity. The first assessment of the literature was conducted using the databases PubMed, CINAHL Plus, Embase, Scopus, MEDLINE, and Web of Science. Subsequently, a search was conducted within the "Cochrane Database of Systematic Reviews (CDSR)" to identify any systematic reviews on the topic that were extant or underway at the time of the search. Various systematic reviews on blood product transfusion and its adverse effects were identified; however, no systematic review studied blood transfusion safety in the paediatric age group or children under 18.

A complete search of the published literature was carried out per the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020" statement [14]. The search for relevant literature was not restricted to a particular country. It was conducted on several databases to prevent missing important research and reduce bias. The searched databases were PubMed, CINAHL Plus, Embase, Scopus, MEDLINE, Web of Science and Cochrane Library. The search in the above databases was undertaken electronically to get the potentially eligible studies that were published between 1st January 2011 and 31st April 2021. A second step was to manually check the reference lists of the currently qualified research to guarantee that no eligible studies were overlooked. The search technique will integrate just terms representing to and referring the participants and the intervention.

The search strategy follows the PICOTT framework [15] (Population, Intervention, Comparator, Outcome, Type of Question, Type of Study) to identify the keywords due to their suitability to assess clinical questions, especially to identify therapy/ intervention effectiveness [16] (Table 1).

Table 1. PICOTT framework

P – Population/Participants	Children who received at least one blood product transfusion. Definition of group: Children
I – Intervention	Blood product or whole blood transfusion
C – Comparator	Whole blood transfusion to no transfusion
O – Outcome	Mortality associated with receipt of blood transfusion Complications during the hospital stay Metabolic complications (hyperkalemia) Transfusion-transmitted infection
T – Type of Question	Prognosis type
T – Type of Study	Interventional and Non-interventional studies; Observational Studies

The search of databases found 4739 articles, and 6 papers were found by harvesting references (Figure 1). Boolean operator combinations and truncations were utilised to narrow down the search results. The MeSH browser was utilised to index articles. The search terms utilized for querying the databases included: "Blood transfusion" and "Transfusion Safety" or "Adverse effects/Transfusion" or "Transfusion reaction" and "Whole blood transfusion" or "Red blood cell transfusion" or "Platelet transfusion" or "Plasma transfusion" or "granulocyte transfusion" and "Pediatrics" or "Children" or "Infants" either singly or in combination. By applying specific search restrictions, the focus of the inquiry was refined to encompass solely primary, peer-reviewed articles accessible in English and available in their entirety.

Study Selection

The inclusion and exclusion criteria are listed in Table 2.

Table 2. Inclusion and exclusion criteria

	Inclusion Criteria	Exclusion Criteria

P – Population/Participants	Children	All others above 18 years of age
	Children who received at least one blood product transfusion.	Children who didn't receive any unit of blood transfusion
I – Intervention	Blood product or whole blood transfusion	Articles did not collect data on blood transfusion
C – Comparator	Whole blood transfusion to no transfusion	Alternative therapies (blood substitutes)
O – Outcome	Mortality following blood transfusion Complications during the hospital stay Metabolic complications (hyperkalemia) Transfusion-transmitted infection	The articles did not collect data regarding the blood transfusion reactions
T – Type of Question	Prognosis type	All articles did not collect data regarding the prognosis-type question
T – Type of Study	Interventional and non-interventional studies Observational Studies Language- English	Meta-analyses and systematic review Case studies with less than 10 participants Articles other than in the English language Literature completed prior to 2011

Before applying the inclusion and exclusion criteria, duplicate studies were removed using the RefWorks tool. Additionally, a manual review was conducted to confirm the elimination of these duplicates, ensuring that no bias resulted from repetition in the study selection process. A total of 4349 publications were found in the literature search after the duplicate articles were removed, and a total of 06 studies were obtained through reference harvesting (Fig 1). 3963 records excluded after title screening. 386 reports were sought for retrieval.

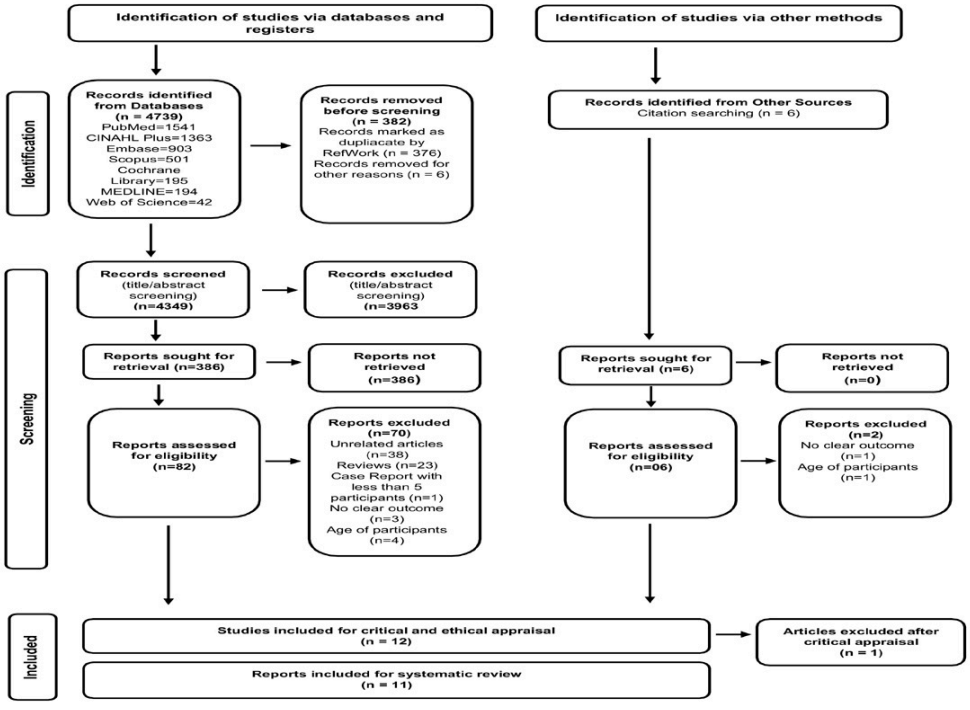

Fig1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [14]

Inclusion Criteria and Exclusion Criteria Implementation

The search results were initially screened for their research design. Following this, the title

And abstract of each paper were scrutinized based on the "P" (Population), "I" (Intervention), "C" (Comparison), "O" (Outcome), "T" (Time), and "T" (Type of Study) criteria for inclusion and exclusion, focusing on studies that were either interventional, non-interventional, or observational in nature. The literature review revealed that in some cases, the population studied was not children, and the intervention employed was alternative therapy rather than blood transfusion. In the next phase of screening, 82 relevant articles on blood transfusion (I-intervention) in children (P-Population) resulted from the search. The full-text articles were reviewed to gather data concerning whether participants received a blood transfusion (C-Comparator). Additionally, these sources were examined for information on complications and mortality rates following blood transfusion (O-Outcome). Articles that provided insufficient or unfocused information regarding blood transfusion were excluded. Following the application of the inclusion and exclusion criteria, a total of 12 papers were selected for the critical appraisal phase (Figure 1 & Table 2).

Critical Appraisal

Various evaluation techniques were used to evaluate the research. Twelve papers were assessed using two critical evaluation techniques to investigate the studies' methodological strengths and flaws as well as their validity and reliability. It was also carried out to determine if the studies had been developed, conducted, and documented adequately and whether they produced a relevant answer to the systematic review issue in question. The cross-sectional study was assessed utilizing the "Appraisal Tool for Cross-Sectional Studies (AXIS)" [17], specifically intended to assess this design. The prospective or retrospective study's quality assessment was conducted using the CASP tool [18]. After the quality check, one study [19] was removed as no definitive conclusion was drawn.

Data Abstraction

Data were extracted from the selected studies in a standardised Microsoft Excel sheet. The following information was extracted: (i) reference (ii) study design (cross-sectional, prospective, retrospective; single centre or multicentre) (iii) study context (clinical setting in which the study was performed) (iv) study period (duration of the study) (v) characteristics of the study population (sample size, health condition) (vi) parameters related to blood transfusion (transfused blood product, primary and secondary outcomes) (vii) aim of the study (vii) results and limitations of the study.

Analysis

This systematic review encompasses data derived from quantitative, non-interventional observational studies. Since the study subject was broad, this evaluation includes papers with various aims and methodologies. It contains six cohort studies, two case-control studies and three cross-sectional studies. Clinical diversity in aspects of PICO is vast in these studies. The population of all studies includes children below 18 years, but the condition of the population is different (immunocompromised, critically ill children, children after surgery) in each study. Likewise, blood products (plasma, platelet, RBC) transferred in each study were different, and the outcomes were also diverse, from mortality to nosocomial infections. A high degree of heterogeneity precluded meta-analysis, and the information was synthesised narratively.

Results

Study characteristics

There were 11 prospective and retrospective observational studies included in the study from various regions throughout the world. Three studies from the USA are single-centre studies [20-22]. 2 studies from Canada are also in a single clinical setting [23,24]. Other single-centre studies are from France [25], Brazil [26], Venezuela [27] and Taiwan [28]. One study from the USA used a multi-institutional registry [22], and another study was conducted in three hospital settings [29]. Another international multicentre study was conducted in 82 PICUs of 16 countries [30]. One study [25] is exclusively for infants below one year, and one study [28] is regarding Extremely low birth weight (ELBW) babies. All nine other studies included children up to 18 years. Two studies were about platelets transfusion [20, 30], two studies were about plasma transfusion [23, 25], and one study discussed all the components of blood [26]. The remaining studies were about RBC transfusion [21, 22, 24, 27-29].

All the studies examined the association between blood product transfused (RBC/platelet/plasma) and the adverse outcome in children or infants. Mortality as the worst outcome was discussed in 5 studies [20, 21, 28-30]. Some studies assessed the association between nosocomial infections and other infections in the post-transfused period [23-25, 27, 28]. Other adverse events reported by various studies include intestinal and neurologic complications [20], new or progressive multiple organ dysfunction syndrome [24] (NPMODS), hypotension, systematic inflammatory response syndrome, acute respiratory distress syndrome [21, 24], prolonged PICU stay [23, 30], venous thromboembolism [22], Necrotizing Enterocolitis (NEC), Retinopathy of prematurity (ROP), bronchopulmonary dysplasia (BPD), late-onset sepsis [28], and Transfusion Associated hyperkalemia [29] (TAH).

Narrative Synthesis

As a result of the narrative synthesis that was performed, the following eight clusters were generated:

01. Platelet transfusion safety
02. Plasma transfusion safety.
03. RBC transfusion safety.
04. Oncology patients under 18yrs.
05. Critically ill children admitted to PICU
06. Injured children less than 15yrs
07. Children underwent surgery
08. Transfusion in infants less than one-year-old

Platelet transfusion safety

The findings of the investigations on platelet transfusion included information on mortality. A case-control study [20] reported that in the pediatric population, there was a single fatality in the group that received platelet transfusion, whereas three deaths were observed in the group that did not receive such transfusion. The fatality in the platelet transfused group (cases) was attributed to significant neurological and gastrointestinal complications. On the other hand, in the non-transfused group, the causes of death were primarily neurological issues, with one case also involving severe gastrointestinal complications, as indicated in the findings [20]. The researchers also looked at serious organ involvement events before and after surgery in individuals who received a platelet transfusion vs those who did not. The study did not observe any statistically significant differences between the groups. The study's principal finding showed no clear differentiation in the severity of acute Post-diarrheal Haemolytic Uremic Syndrome (D + HUS) between children who got platelet transfusions and those who did not [20]. Contrary to this study, another multicentre investigation [30] found that the total platelet dosage provided was independently related to higher ICU mortality. Overall, the mortality rate in the Intensive Care Unit (ICU) was 25%, but this varied from 18% to 35%, depending on the specific reason for the blood transfusion [30]. Most platelet transfusions were administered to nonbleeding kids as a preventative measure, and platelet thresholds vary significantly [30].

Plasma transfusion safety.

This review includes two papers that look at the consequences of plasma transfusion. The first was a single-centre observational study [25]. The study examines the hypothesis that administering plasma transfusions after cardiac surgery is associated with an increased incidence of Nosocomial Infections (NI) during the patient's stay in the Pediatric Intensive Care Unit (PICU). Plasma transfusion following cardiac surgery with Cardiopulmonary Bypass (CPB) was not shown a significant association for the development of NIs in children younger than one year old who were hospitalised in the PICU [25]. However, a separate study conducted at a single center investigates the relationship between plasma transfusions and the clinical outcomes of critically ill pediatric patients [23]. The findings show a substantial and independent link between plasma transfusions and higher morbidity [23]. The study showed that patients who received at least one plasma unit had a substantially increased risk of having new or worsening Multiple Organ dysfunction syndrome (MODS), developing hospital-acquired infections, and spending more time in the PICU [23].

RBC transfusion safety

The transfusion of red blood cells (RBCs) is the most frequent blood product transfusion. This review examined six research for their findings on RBC transfusion in children. RBC transfusion has been associated with worse results in all of the studies. A study aimed at identifying the adverse effects of Red Blood Cell (RBC) transfusion within a diverse Pediatric Intensive Care Unit (PICU) population uncovered a correlation indicating that RBC transfusion is independently associated with heightened morbidity [24]. This association includes a heightened risk of developing New or Progressive Multiple Organ Dysfunction Syndrome (NPMODS), extended durations of PICU stay, and prolonged periods of mechanical ventilation [24]. RBC transfusion was identified as an independent risk factor for nosocomial infections in medical and surgical care centres that provided treatment to critically sick children in another research [27]. According to another study conducted among juvenile trauma patients, early pRBC transfusion was related to a 50% increase in death [21]. Compared to individuals who did not get pRBC transfusion, those who received it late had more extended ICU stays and more ventilator days [21]. When RBC transfusion is performed during surgery, there is an elevated risk of postoperative VTE in paediatric patients; however, this risk is still shallow [22]. A study [28] concluded that the administration of RBCs to ELBW newborns was shown to be related to an increased risk of neonatal mortality. It also established a relationship between RBC transfusion and a higher likelihood of ROP threshold [28]. However, this research found that RBC transfusion positively influenced late cognitive development in ELBW babies, as measured by the MDI score at 18-24 months corrected age in ELBW infants [28]. The frequency of TAH in children who had RBC transfusions was modest (0.93 percent, suggesting that 1 out of every 108 kids in the study developed TAH); nonetheless, the 1-day death rate was 20% in this group of children [29]. A multitude of circumstances caused TAH, and all of the patients in that study had comorbidities that might increase TAH and associated complications [29].

Oncology patients

The transfusion response profile of paediatric oncology patients was investigated in a study. 55.5% of patients with transfusion reactions were between the ages of 10 and 18, 94.4% were poly-transfused, and 62.3% had no previous history of a transfusion reaction [26]. The transfusion profile showed a high prevalence of urticaria, erythema, and fever, as well as acute allergic-type reactions associated with platelet transfusion [26]. The research also indicated that if they detect a transfusion response, they should promptly cease the transfusion and act to prevent the complication [26].

Critically ill children admitted to PICU

A study in severely ill children found a substantial and independent link between blood product (plasma) transfusions and higher morbidity [23]. One study [24] reported that RBC transfusions in severely sick infants were related to extended mechanical ventilation and PICU duration. The study further [24] doubts the capacity of preserved RBCs to enhance oxygenation in critically unwell infants. Outcomes such as mortality and NI has also shown an association with blood transfusion in two studies [27, 30].

Injured children

Among children younger than 15 years of age, three-year research looked into the relationship between transfusion and increased morbidity and mortality in wounded children [21]. A pRBC transfusion was given to 8% of the injured kids (43/512). Roughly half of the children who received an early packed Red Blood Cell (pRBC) transfusion following injury succumbed to their injuries. However, it's important to note that the majority of these fatalities were attributed to injuries involving the central nervous system [21]. The number of days spent on the ventilator and in the critical care unit was higher in children who had pRBC transfusions than those who did not [21]. In this study, uncontrolled bleeding and coagulopathy were associated with early post-injury mortality following pRBC transfusion [21].

Children underwent surgery

According to the findings of one research, the use of perioperative RBC transfusions in paediatric surgical patients was related to an increased incidence of postoperative VTE [22]. This relationship remained significant despite accounting for other potential prothrombotic risk factors [22

]. In children who have surgery and need RBC transfusions during the surgery, this study says they should be closely watched and given a lower threshold for mechanical and chemical prophylaxis [22]. Children younger than 1 year old who had heart surgery and received plasma had a higher risk of getting bloodstream infections, mediastinitis, and other infections in the hospital [25]. The study was only done at one location [25], making the findings less generalisable. In the case of children who underwent cardiac surgery, the decision to administer plasma transfusions was made at the discretion of the attending physicians, based on individual patient assessments. There was no standardized protocol or guideline uniformly applied to these decisions [25].

Transfusion in infants less than one-year-old

Blood transfusion is frequently regarded as a life-saving intervention in highly sick neonates. Most blood transfusions are given to the tiniest and most immature newborns [28]. Hospital mortality and short-term morbidity have been linked to RBC transfusions in neonates [28]. However, in ELBW preterm newborns, the relationship was beneficial in later neurodevelopmental outcomes [28]. In another centre, plasma transfusion following heart surgery in babies younger than one year of age was shown not to affect the outcomes of the patients [25].

Discussion

A total of 11 papers were found in this systematic review that documented safety associated with different blood product transfusion practices in children. The objective of this research was to provide a comprehensive overview of all documented concerns to understand better the clinical adverse reactions and associations linked to blood transfusions.

Paediatric patients' reactions to blood products

The paediatric patient's reaction to various blood products is different in different contexts. The transfusion outcome depends on the comorbidities and the patient's current health condition. This review noted that the blood transfusion led to mortality, nosocomial infection, MODS, venous thromboembolism, NEC, ROP, BPD, and late-onset sepsis. TAH was seen in individuals who also had other concomitant conditions. In addition to these, intestinal and neurological complications, prolonged ICU stay and 28-day mortality, hypotension, systemic inflammatory response syndrome, and acute respiratory distress syndrome were noted as secondary outcomes.

Need for long-term studies in the vulnerable population

The review establishes an association between harmful outcomes and children exposed to RBC, platelet and plasma transfusion practices. On the contrary, two studies could not show an association (plasma and platelet) with the outcomes [20, 25]. There were no statistically significant differences in various adverse effects between children exposed to blood transfusion procedures and those not exposed to it [31]. Nevertheless, the presence of risk of bias identified in numerous studies, combined with the inconsistency in reporting and the lack of uniform definitions for various occurrences, limits the reliability of the conclusions that can be derived from these investigations.

Blood transfusions have been linked with adverse outcomes in critically ill pediatric patients. In severely ill children, plasma and platelet transfusions are related to increased organ failure and death. Despite the possibility of therapeutic advantages, haemostatic transfusions are accompanied by poorer clinical results in the long run. Platelet transfusions were the most often related to transfusion responses in adult and paediatric groups, followed by RBC transfusions and then plasma transfusions [6]. When comparing the paediatric population to the general adult population, there is an overall rise in transfusion responses.

The transfusion profile of oncology patients showed a high prevalence of urticaria, erythema, fever, and acute allergic-type reactions associated with platelet transfusion [26]. Other studies supported these findings. Allergic responses to platelets and RBCs were the paediatric group's most often testified reaction forms. A higher than threefold increase in the rate of allergic reactions to platelets was seen in children than in adults, and a greater than sevenfold increase in the incidence of allergic reactions to RBCs was observed in children compared to adults [7]. According to the findings of this investigation, critically ill children are more prone than adults to respond to blood products, with RBC and platelet transfusions being linked with the most significant magnitude of observed differences. Long-term studies in the vulnerable population (immune-compromised and critically ill children) should be encouraged to reduce the worst outcome.

Long-term effects of blood transfusion reaction in children

Metabolic complications of blood transfusion remain unnoticed on some occasions. Because young children may have difficulties communicating their symptoms to healthcare practitioners, this finding may be explained by the fact that the clinician must define the reaction solely based on physically visible signs. Transfusion-associated Hyperkalaemia may be more prevalent in juvenile populations, which fall into this category. The frequency of TAH in children who had RBC transfusions was modest, and a multitude of circumstances caused TAH [29]. It could also be a sign that medical staff would be too careful when giving RBC products to children, leading to a reaction report that doesn't meet any case definition criteria [7].

According to the findings of one research, the use of perioperative RBC transfusions in paediatric surgical patients was related to an increased incidence of postoperative VTE [22]. Another study [32] confirmed by confirmed that children, infants, and neonates who get preoperative RBC transfusions are more likely to have new or worsening VTE after surgery [32]. Another study also observed various transfusion reactions over two years in a PICU in a study and noted increased mortality [33]. There are no studies with a well-developed follow-up or information on the long-term consequences of blood transfusions in children. Improvements in the observation of transfusions administered to patients in the PICU and improved understanding of these responses among healthcare workers should help to enhance the safety of transfusions in the PICU.

Various alterations to familiarise and standardise children's adverse transfusion reaction

This review noted that post-surgical children who needed blood transfusion should be closely watched and given a lower threshold for mechanical and chemical prophylaxis [22]. An additional risk factor related to RBCT is the duration of the procedure, haemorrhage, and oxygen saturation levels. These considerations should be considered when planning paediatric treatments, particularly where exposure to RBCT is desired [34]. De Pascale, et al., reported that apheresis of platelet and RBC showed more excellent transfusion safety [35]. Other studies also supported blood product modification. Modifications to blood products can significantly reduce the dangers associated with transfusions [3]. They have also proposed leukoreduction, irradiation, washing, volume reduction, pathogen inactivation, and other treatments [3]. Alteration of the blood product can improve transfusion safety by reducing the risk of infection. More research, however, is needed to determine the safety of each alteration for each kind of blood product in question. Every alteration is unique, and it will behave uniquely with every blood product.

Develop new health data and strategies to increase safety

A significant incidence of transfusion reactions in children is seen, which depends on the following variables: the kind of blood component administered, patient comorbidity, and the number of transfusions received; the sort of response is also connected with the type of blood component and the age of the patient [36]. The understanding of patients and the variables that contribute to transfusion responses serve as the foundation for the development of preventative measures, which ultimately contribute to improving the transfusion services and care provided to patients.

It is estimated that current transfusion practices partially comply with suggested transfusion standards. Guidelines for transfusions in children are based primarily on "professional opinion" instead of scientific proof. Similar to transfusion practices in adults, current methods of blood transfusion in pediatric settings often fail to incorporate the application of existing knowledge regarding the need for transfusions. There is a pressing need for more rigorous efforts to adopt and implement evidence-based transfusion practices in the treatment of children. New health data and strategies should implement to increase the safety from adverse transfusion reactions in young children

Limitations of the study

Given several studies identified, the research quality that has provided primary and secondary outcomes has been low. Numerous studies were likely to have been compromised by confounding due to indication bias. More severely sick babies were more likely to have a blood transfusion than the rest of the population. Furthermore, the sample sizes in many research are from a single centre, which is insufficient for addressing damage comprehensively. This review included only articles published in English, which might give rise to selection bias. Some reports did not mention

The age of the children and those articles were skipped from the review. Data from those articles might contribute to reasonable interpretations. This review included studies with the retrospective/prospective nature of the data analysis. These observational studies are capable of identifying an independent association, but they are not equipped to establish a cause-and-effect relationship between blood transfusions and clinical outcomes in pediatric patients. To definitively ascertain such a causal relationship, a randomized clinical trial is required.

Conclusion

Acute and chronic diseases usually necessitate blood transfusions. This systematic study emphasizes paediatric transfusion responses and shows that the incidence of transfusion reactions among the paediatric population is on the rise. The findings of this review indicate that further clinical studies with specified criteria for adverse events are required to settle the uncertainty surrounding the safety of blood transfusion in a population with relative immunologic immaturity. Even though the current data do not support the safety of transfusion triggers, they do highlight the significance of future investigation. Performing a randomised trial with a bigger number of patients, in my opinion, would be beneficial in order to recommend other techniques for establishing more precise criteria for preventing hazardous acute responses in paediatric patients who are transfusion dependent. The need for more research to explain suitable indications and the introduction of standardised protocols for the blood transfusion process and subsequent reactions in critically sick children are considered necessary.

Supporting information

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Ethical Considerations

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Author contribution statement

Ancy Chandrababu Mercy Bai: Conceptualization (lead); writing – original draft (lead); formal analysis (lead); writing – review and editing (equal). **Divya Vinnakota**: conceptualization, Software (lead); writing – review and editing (equal). **Abu Rushd Mohammad Mashrur**: conceptualization, Resources; writing – review and editing (equal). **Sumana Choudhury**: conceptualization, Software (lead); writing – review and editing (equal). **Ajoy Kumer Ghosh**: conceptualization, Software (lead); writing – review and editing (equal). **Russell Kabir**: Conceptualization (lead); writing – original draft (lead); formal analysis (lead); writing – review and editing (equal).

All authors attest they meet the ICMJE criteria for authorship and gave final approval for submission.

Data availability statement

Data included in article/supp. material/referenced in article.

Additional information

No additional information is available for this paper.

Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. WHO. WHO Action framework to advance universal access to safe, effective and quality assured blood products. Available from: https://www. *who.int/publications/i/item/action-framework-to-advance-uas-bloodprods-978-92-4-000038-4; 2020. Accessed Jan 11, 2022 [Crossref][PubMed][Google Scholar]*

2. Frazier SK, Higgins J, Bugajski A, Jones AR, Brown MR. Adverse Reactions to Transfusion of Blood Products and Best Practices for Prevention. Crit Care Nurs Clin North Am 2017;29(3):271-290. *[Crossref][PubMed][Google Scholar]*

3. Raval JS, Griggs JR, Fleg A. Blood Product Transfusion in Adults: Indications, Adverse Reactions, and Modifications. Am Fam Physician 2020;102(1):30-38. *[Crossref][PubMed][Google Scholar]*

4. Chang T. Transfusion Therapy in Critically Ill Children. Pediatrics and neonatology; Pediatr Neonatol 2008;49(2):5-12. *[Crossref][PubMed][Google Scholar]*

5. Slonim AD, Joseph JG, Turenne WM, Sharangpani A, Luban NLC. Blood transfusions in children: a multi-institutional analysis of practices and complications. Transfusion 2008;48(1):73-80. *[Crossref][PubMed][Google Scholar]*

6. Oakley FD, Woods M, Arnold S, Young PP. Transfusion reactions in pediatric compared with adult patients: a look at rate, reaction type, and associated products: Epidemiology of Transfusion Reactions in Pediatric Patients. Transfusion (Philadelphia, Pa. *) 2015;55(3):563-570 [Crossref][PubMed][Google Scholar]*

7. Vossoughi S, Perez G, Whitaker BI, Fung MK, Stotler B. Analysis of pediatric adverse reactions to transfusions. Transfusion 2018;58(1):60-69. *[Crossref][PubMed][Google Scholar]*

8. Perel Y, Runel C, Huguenin Y, Renesme L, Aladjidi N. Transfusion and its specific problems in pediatrics and neonatology. Transfusion clinique et biologique : journal de la Société française de transfusion sanguine 2017;24(3):101. *[Crossref][PubMed][Google Scholar]*

9. Vichinsky E, Neumayr L, Trimble S, Giardina PJ, Cohen AR, Coates T, et al. Transfusion complications in thalassemia patients: a report from the Centers for Disease Control and Prevention (CME): Transfusion Complications in Thalassemia. Transfusion (Philadelphia, Pa. *) 2014;54(4):972-981 [Crossref][PubMed][Google Scholar]*

10. Jacquot C, Delaney M. Pathogen-inactivated blood products for pediatric patients: blood safety, patient safety, or both? Transfusion 2018;58(9):2095-2101. . *[Crossref][PubMed][Google Scholar]*

11. Moncharmont P. Adverse transfusion reactions in transfused children. Transfus Clin Biol 2019;26(4):329-335. *[Crossref][PubMed][Google Scholar]*

12. Harris JC, Crookston KP. Blood Product Safety. Available from: https://www. *ncbi.nlm.nih.gov/books/NBK539826/?report=classic; 2021. Accessed May 16, 2021 [Crossref][PubMed][Google Scholar]*

13. McLean J, M. D. Health Care-Associated Infection After Red Blood Cell Transfusion: A Systematic Review and Meta-analysis. *J Emerg Med 2014;47(1):130 [Crossref][PubMed][Google Scholar]*

14. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. *[Crossref][PubMed][Google Scholar]*

15. Richardson WS, Wilson MC, Nishikawa F, Hayward RS. The well-built clinical question: a key to evidence-based decisions. ACP Journal Club. *1995;123(12):12-13 [Crossref][PubMed][Google Scholar]*

16. Integrating the framing of clinical questions via PICO into the retrieval of medical literature for systematic reviews. Information and Knowledge Management; Nov 8-10, 2017; New York: Association for Computing Machinery; 2017. . *[Crossref][PubMed][Google Scholar]*

17. Downes MJ, Brennan ML, Williams HC, Dean RS. Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). BMJ Open 2016;6(12):e011458. *[Crossref][PubMed][Google Scholar]*

18. Critical Appraisal Skills Programme. CASP Case Control Study Checklist. 2018; Available at: https://casp-uk. *b-cdn.net/wp-content/uploads/2018/03/CASP-Case-Control-Study-Checklist-2018_fillable_form.pdf; 2018. Accessed May 14, 2021 [Crossref][PubMed][Google Scholar]*

19. Karam O, Demaret P, Shefler A, Leteurtre S, Spinella PC, Stanworth SJ, et al. Indications and Effects of Plasma Transfusions in Critically Ill Children. Am J Respir Crit Care Med. *2015;191(12):1395-1402 [Crossref][PubMed][Google Scholar]*

20. Balestracci A, Martin SM, Toledo I, Alvarado C, Wainsztein RE. Impact of platelet transfusions in children with post-diarrheal hemolytic uremic syndrome. Pediatr Nephrol. *2013;28(6):919-925 [Crossref][PubMed][Google Scholar]*

21. Pieracci FM, Witt J, Moore EE, Burlew CC, Johnson J, Biffl WL, et al. Early death and late morbidity after blood transfusion of injured children: a pilot study. J Pediatr Surg. *2012;47(8):1587-1591 [Crossref][PubMed][Google Scholar]*

22. Rothstein DH, Cairo SB, Schaefer BA, Lautz TB. Association of perioperative red blood cell transfusion with postoperative venous thromboembolism in pediatric patients: A propensity score matched analysis. Pediatr Blood Cancer. *2019;66(10):e27919 [Crossref][PubMed][Google Scholar]*

23. Karam O, Lacroix J, Robitaille N, Rimensberger PC, Tucci M. Association between plasma transfusions and clinical outcome in critically ill children: a prospective observational study. Vox Sang. *2013;104(4):342-349 [Crossref][PubMed][Google Scholar]*

24. Demaret P, Tucci M, Karam O, Trottier H, Ducruet T, Lacroix J. Clinical outcomes associated with RBC transfusions in critically ill children: A 1-year prospective study. Pediatr Crit Care Med. *2015;16(6):505-514 [Crossref][PubMed][Google Scholar]*

25. Chenouard A, Rozé J-, Hanf M, Macher J, Liet J-, Gournay V, et al. Evaluation of the relationship between plasma transfusion and nosocomial infection after cardiac surgery in children younger than 1 year. Pediatr Crit Care Med. *2015;16(2):139-145 [Crossref][PubMed][Google Scholar]*

26. Vital de Freitas J, de Almeida PC, Vilani Cavalcante Guedes M. Transfusion Reactions Profile in Oncology Pediatrics Patients. J Nurs UFPE on line. *2014;8(7):3030-8 [Crossref][PubMed][Google Scholar]*

27. Naveda Romero OE, Naveda Meléndez AF. Are red blood cell transfusions associated with nosocomial infections in critically ill children? Arch Argent Pediatr. 2016;114(4):347-351. *[Crossref][PubMed][Google Scholar]*

28. Wang YC, Chan OW, Chiang MC, Yang PH, Chu SM, Hsu JF, et al. Red Blood Cell Transfusion and Clinical Outcomes in Extremely Low Birth Weight Preterm Infants. Pediatr Neonatol. *2017;58(3):216-222 [Crossref][PubMed][Google Scholar]*

29. Yamada C, Edelson M, Lee A, Saifee NH, Bahar B, Delaney M. Transfusion-associated hyperkalemia in pediatric population: Prevalence, risk factors, survival, infusion rate, and RBC unit features. Transfusion. *2021;61(4):1093-1101 [Crossref][PubMed][Google Scholar]*

30. Nellis ME, Karam O, Mauer E, Cushing MM, Davis PJ, Steiner ME, et al. Platelet Transfusion Practices in Critically Ill Children. Crit Care Med. *2018;46(8):1309-1317 [Crossref][PubMed][Google Scholar]*

31. Keir A, Pal S, Trivella M, Lieberman L, Callum J, Shehata N, et al. Adverse effects of red blood cell transfusions in neonates: a systematic review and meta-analysis. Transfusion. *2016;56(11):2773-2780 [Crossref][PubMed][Google Scholar]*

32. Goel R, Josephson CD, Patel EU, Petersen MR, Makhani S, Frank SM, et al. Perioperative transfusions and venous thromboembolism. Pediatrics. *2020;145(4):e20192351 [Crossref] [PubMed][Google Scholar]*

33. Gauvin F, Lacroix J, Robillard P, Lapointe H, Hume H. Acute transfusion reactions in the pediatric intensive care unit. Transfusion. *2006;46(11):1899-1908 [Crossref][PubMed][Google Scholar]*

34. Ligon RA, Downey LA, Gruenewald DL, Bauser-Heaton H, Kim DW, Roman MF, et al. Risk Factors for Red Blood Cell Transfusions in Children Undergoing Cardiac Catheterization. J Pediatr. *2020;217:25-32.e4 [Crossref][PubMed][Google Scholar]*

35. De Pascale MR, Belsito A, Sommese L, Signoriello S, Sorriento A, Vasco M, et al. Blood transfusions and adverse acute events: A retrospective study from 214 transfusion-dependent pediatric patients comparing transfused blood components by apheresis or by whole blood. Ann I Super Sanita. *2019;55(4):351-356 [Crossref][PubMed][Google Scholar]*

36. Pedrosa AKKV, Pinto FJM, Lins LDB, Deus GM. Blood transfusion reactions in children: associated factors. J Pediatr. *2013;89(4):400-406 [Crossref][PubMed][Google Scholar]*

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